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CORRESPONDENCE

Research Correspondence

Histopathological Features of Delayed Enhancement Cardiovascular Magnetic Resonance in Isolated Left Ventricular Noncompaction

To the Editor: Contrast-enhanced magnetic resonance imaging (CE-MRI) is an important imaging modality for the evaluation of isolated left ventricular noncompaction (LVNC). The delayed gadolinium enhancement has been identified in both compacted and noncompacted myocardium, and it may correlate with the clinical severity of LVNC (1–3). However, little is known about the histological basis of myocardial delayed enhancement in LVNC patients, especially in the noncompacted myocardium. In this study, we made a comparison between the myocardial delayed enhancement and histological findings in a patient with LVNC who underwent heart transplantation.

A 27-year-old man was admitted with exertional dyspnea. Chest roentgenogram showed cardiomegaly with pulmonary venous congestion, and the cardiothoracic ratio was 72%. The LVNC was diagnosed by echocardiography, and the ratio of the noncompacted to compacted myocardium was 3.2. The left ventricular end-diastolic dimension was 63 mm, and left ventricular ejection fraction was 18%. Contrast-enhanced MRI was performed, and deep intertrabecular recesses presented in the apical and lateral wall of the left ventricle. The near-transmural delayed enhancement occurred in the interventricular septum, and diffuse enhancement presented in the free wall and the trabecular meshwork region of the left ventricle. In addition, CE-MRI detected the left ventricular thrombus and pericardial and pleural effusions. One week later, informed consent was obtained, and heart transplantation was carried out. The pathological findings of the explanted heart were compared with the previous in vivo CE-MRI (Fig. 1). In the compacted myocardium with delayed enhancement, extensive fibrosis was identified and predominantly localized in the mid-myocardial wall. The collagen volume fraction was 27.9% in the histological section, which came from the region of near-transmural delayed enhancement in the interventricular septum. In the noncompacted myocardium with delayed enhancement (the trabecular meshwork region of left ventricle), however, 2 types of pathological findings presented: mucoid degeneration in the endocardium and fibrosis within the trabeculations. The collagen volume fraction of trabeculations was 37.4% in the left ventricular apex and 32.8% in the lateral wall of the left ventricle. In the myocardial regions without delayed enhancement, there was no significant increase in the amount of fibrosis. The epicardial coronary arteries were normal in the patient.

The results of this study demonstrated that fibrosis was identified histologically in both compacted and noncompacted myocardium. In the compacted myocardium, the regions of delayed enhancement corresponded well with the focally increased fibrosis. Furthermore, CE-MRI may overestimate the degree of fibrosis replacement, as we found in the interventricular septum. In the noncompacted myocardium, delayed enhancement was associated with fibrosis within the trabeculations as well as mucoid degeneration in the endocardium.

Previous studies have showed that myocardial delayed enhancement presented in patients with LVNC, and it has been proposed that the regions of delayed enhancement probably reflected the regions of increased myocardial fibrosis (1,2). Pathological analysis also demonstrated that fibrosis occurred in the left ventricular myocardium of LVNC patients (4,5). However, further research

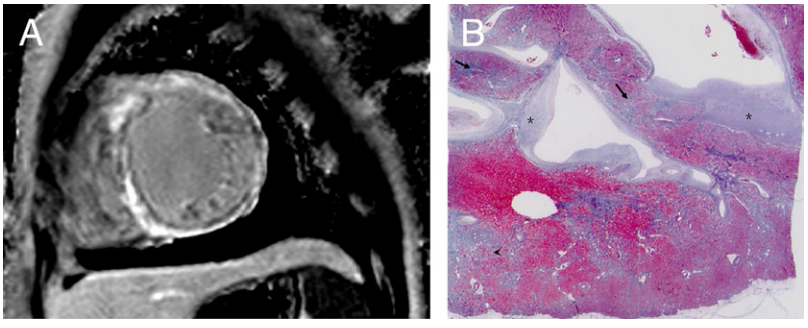

Figure 1 **Comparison of In Vivo CE-MRI and Histological Sections in LVNC**

(A) Contrast-enhanced magnetic resonance imaging (CE-MRI) in short-axis view demonstrated that diffuse delayed enhancement occurred in the interventricular septum, left ventricular free wall, and the trabecular meshwork region of the left ventricle. **(B)** The histological section in isolated left ventricular noncompaction (LVNC) from the apical segment of the left ventricle demonstrated that fibrosis presented within trabeculations **(arrow)** as well as in compacted myocardium **(arrowhead)**. In addition, mucoid degeneration **(asterisk)** was identified in endocardium. (Masson's Trichrome stain, original magnification ×1).

was lacking to assess the histopathological correlation of myocardial delayed enhancement in LVNC. In the present study, our findings show that the fibrosis is the histological basis in the delayed enhancement of compacted myocardium; however, it is still unknown which mechanism plays the leading role in the delayed enhancement of noncompacted myocardium.

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Please note: This study was approved by the hospital research ethics committee.

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Letters to the Editor

Diagnostic Criteria for Percutaneous Coronary Intervention-Related Myocardial Infarction

Time for Revision?

A significant increase of cardiac biomarkers after percutaneous coronary intervention (PCI) is commonplace and is thought to reflect a clinically significant myocardial injury. According to the joint European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation task force for the redefinition of myocardial infarction (MI), increases of cardiac troponins >3 times the 99th percentile upper reference limit (URL) are designated as percutaneous coronary intervention (PCI)-related MI (type 4a) (1).

We read with interest the article by Lim et al. (2), who concluded that creatine kinase-myocardial band (CK-MB) should be the preferred biomarker when applying the current universal definition of MI to periprocedural injury, because the arbitrary limit of 3 times the 99th percentile URL troponin threshold might be oversensitive and lead to over-diagnosis of MI in as many as 53% of patients (2). A similar conclusion was earlier reached by Locca et al. (3), who reported a lack of substantial agreement between the new universal definition and cardiovascular magnetic resonance for the diagnosis of small-size periprocedural myocardial damage after complex PCI (3). Although the current definition of periprocedural injury based on the >3 times the 99th percentile URL troponin value might, hence, be challenging, especially when using the new highly sensitive assays, Testa et al. (4) carried out a meta-analysis of 15 studies and 7,578 patients, concluding that troponin elevation was observed in 28.7% of patients undergoing PCI, whereas the incidence of PCI-related MI according to the new definition was 14.5% (4). Most importantly, any level of raised troponin was associated with an increased risk of the composite of all-cause death, MI, repeat target vessel PCI, and coronary artery bypass graft surgery.

Taken together, this evidence suggests that the arbitrary limit of 3 times the 99th percentile URL troponin threshold for diagnosing periprocedural injury might be urgently revised, because of 1) the unsatisfactory diagnostic specificity at this low level; and 2) the potentially inaccurate selection of the reference population for calculating the URL (5). Therefore, a higher cut-off—such as that suggested by Lim et al. (i.e., 40 times the 99th percentile)—should be used for diagnosing periprocedural MI. This enhanced threshold not only displays diagnostic performances comparable to that of CK-MB, but also overcomes the use of a double-biomarker approach (i.e., troponin and CK-MB), with a substantial economical saving. Nevertheless, the current threshold has meaningful prognostic implications, so that patients with troponin values between 3 and 40 times the 99th percentile are to be considered at risk of adverse events and should be managed accordingly.

It is also noteworthy that sample stability is critical for troponin testing. Wu et al. (6) recently observed variations in troponin I above the analytical precision cut-off (as measured with a high-sensitivity assay) in 17% of short-term and 33% of long-term storage samples, suggesting that measurements are more accurate when fresh samples are used, suggesting that the definition of the optimal thresholds for both defining an increased risk of adverse events and diagnosing MI after periprocedural injury should be made preferably using fresh samples.

We are actually trapped between the Scylla of the universal definition of MI and the Charybdis of the prognostic implications